Lipids and Diabetes: a Fatal Combination?

Lipids have for a long time been the Cinderella of diabetes care. Lipidologists have tended to be a small, happy band of proselytizing zealots who were wheeled out for State of the Art lecturers, applauded and returned thankfully to their laboratories. Lipid metabolism was (and still is) complex, with bewildering slides of metabolic pathways, reminiscent of distorted maps of the London Underground. Diabetologists hid gratefully behind the *ex cathedra* statement that it was not worth measuring lipids in the non-fasting state and that lipids 'got better' if blood glucose was well controlled.

Over the past few years, the situation has changed dramatically. Type 2 diabetic patients have a much enhanced chance of developing macrovascular disease and ischaemic heart disease in particular is causally related to lipid patterns. Not only do Type 2 patients have high LDL-cholesterol levels; they also have the combination of raised triglycerides and low HDL-cholesterol. This latter combination appears to be a particularly important risk predictor in diabetes, as shown in the Scandinavian 4S study.[1,2] It is also clear that once fasting triglyceride levels exceed 1.5 mmol l^{-1}, small dense LDL particles predominate, rather than the less atherogenic normal less dense LDL. Furthermore, LDL may be glycated in the face of raised blood glucose levels and glycated LDL is more likely to be cleared by the macrophage scavenger pathway, another risk factor for atherogenesis.

Much of the rebirth of interest in lipids has come from the recognition of 'Sydrome X' or the 'Metabolic Syndrome'—a clustering of cardiovascular risk factors including abnormal glucose tolerance, obesity (particularly of the central variety), hypertension and raised triglycerides, with insulin resistance as a common unifying factor. Certainly, raised triglycerides can cause insulin resistance, as shown in many acute studies.

What remains to be proven is whether lowering of serum lipid levels, particularly of triglycerides, has benefit in decreasing cardiovascular disease specifically in those with diabetes. There are hints that this may be so, but the results of the definitive studies currently underway are required. Added weight is given by the article of Fiorkowski *et al*. in this issue,[3] who have found that total cholesterol is a better predictor of overall mortality than glycaemic control in Type 2 diabetes.

The other aspect of lipid metabolism which has perhaps received too little attention is the role of non-esterified ('free') fatty acids (NEFA). Philip Randle and co-workers first suggested that NEFA were important in the regulation of glucose metabolism more than 30 years ago. He perceptively suggested that raised NEFA could be instrumental in causing the insulin resistance which is now recognised as a fundamental component of Type 2 diabetes. Interest in this concept was rekindled during the past decade when the pathophysiology of insulin resistance came under scrutiny. It was shown that lowering NEFA could improve insulin sensitivity. More recently, the possible role of NEFA released from omental adipocytes in the Metabolic Syndrome has been investigated. In this issue of *Diabetic Medicine*, Paolisso and Howard examine the possible role of NEFA as aetiological factors for Type 2 diabetes both through causing insulin resistance and impairing insulin secretion.[4]

So what should the practising diabetologist do? It is too early to suggest routine measurement of plasma NEFA, with a view to active management. However, regular assessment of cholesterol and triglycerides, available from every clinical laboratory service, should be carried out—annually at least and more often if values are elevated. It is not enough to assume that lipid levels will be normalised if blood glucose levels are lowered—they will not. Specific action must be taken—first by careful attention to diet and then with drugs if necessary. Fibrates are particularly useful if triglycerides are elevated, with statins in cases of isolated elevation of LDL cholesterol. Cardiovascular disease remains the main cause of (premature) death in Type 2 diabetes and all risk factors require attention. This most certainly includes the lipids.

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References

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